## REMARKS

Claims 23 and 26 have been amended. No new matter has been added. Support for the amendments to claim 23 can be found, for example at the originally filed claims. Support for the amendments to claim 26 can be found in the accompanying declaration attached at Appendix A and the receipt of the deposit of the hybridoma attached at Appendix B.

Claims 23-28 are pending.

## SPECIFICATION

The Examiner has objected to the disclosure and has requested that Applicants provide the assurance statement for the hybridoma cell line deposited in the Advanced Biotechnology Center Inter Lab Line collection (CBA ICLB) in the content of the specification. See Office Action at p. 2. Applicants have amended the specification on p. 9 to incorporate the deposit number, the date of the deposit, the address of the depository and the statement that the deposit was made under the terms of the Budapest Treaty. Applicants respectfully request the withdrawal of this objection.

## CLAIM REJECTIONS

***Rejection under 35 U.S.C. § 10i***

The Examiner has rejected claim 23 as being directed to non-statutory subject matter. See Office Action at p. 2. Specifically, the Examiner states that "[t]here is no recitation of isolation or synthesis in front of the claimed antibody" and recommends that Applicants incorporate "isolated or synthesized" to the claim language. Applicants thank the Examiner for the recommendation. Claim 23 has been amended incorporate the claim language "isolated or synthesized" in front of the claimed antibody. Applicants respectfully request that the withdrawal of this rejection.

***Rejection under 35 U.S.C. § 112, first paragraph***

***Claims 24-25***

The Examiner has rejected claims 24-25 under 35 U.S.C. § 112, first paragraph, for lack of enablement. See Office Action at p. 3. Specifically, the Examiner states that the specification while enabling for "having an isolated monoclonal antibody DB-81 that is able to inhibit the HIV envelope protein mediated fusion with CD4+ T cells, does not reasonably provide enablement

for using any antibody binding to a fixed cell expressing any HIV-1 envelope protein gp120 that forms a complex with soluble CD4 (sCD4) in any host cell for treating and preventing an HIV infection for any type, strains or isolates." Id. Applicants respectfully traverse this rejection.

The specification adequately describes and enables a method of treating or preventing HIV infection or a method of treating or preventing a disease or condition of, or related to, the immune system using an isolated or synthesized antibody immunospecific for a fixed cell comprising an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor. See for example, Example 4-5 on pages 42-43 of the specification which describes the inhibition of HIV-1 envelope-mediated cell fusion and inhibition of cell fusion mediated by diverse HIV-1 envelopes. The specification further describes evaluating antibody DB-81 *in vitro* for its capability to interfere with HIV-1 dependent cell fusion using cell lines expressing envelopes from biologically diverse viral isolates and HIV-1 replication in primary peripheral blood cells. See p. 44, line 40 to p. 45, line 2 of the specification. In addition, the specification also describes the ability of DB-81 to interfere with HIV-1 dependent cell fusion in Example 9 (p. 45-46) as well as the anti-inflammatory properties of DB-81 (see Example 10, p. 46 of the specification). In Example 9, the specification describes effector cells infected with vaccinia vectors expressing biologically different HIV-1 envelopes which were then mixed with target cells infected with vaccinia vectors expressing the appropriate coreceptor, i.e. NIH3T3-CCR5 or HeLa-CXCR4 and CD4. See p. 45 of the specification. Results of the effects of DB-81 are shown in Figure 7 and demonstrate the ability of DB-81 to interfere with HIV-1 dependent cell fusion.

Thus, Applicants have informed and demonstrated to a person having ordinary skill in the art how to use the invention commensurate in scope with the claims. As such, Applicants respectfully request reconsideration and withdrawal of this rejection with respect to claims 24 and 25.

***Claims 23-28***

The Examiner has rejected claims 23-28 under 35 U.S.C. § 112, first paragraph for failing to comply with the enablement requirement. See Office Action at p. 5. The Examiner states that "the specification does not provide a repeatable method for obtaining said antibody or hybridoma cell line, and it does not appear to be readily available material." Id. The Examiner however, states that "[d]eposit of said hybridoma cell line would satisfy the enablement requirements of 35

U.S.C. 112" and that "Applicant's deposit statement on specification page 45 does not indicate the extent of public availability." Id.

Applicants herein provide a declaration by Dr. Samuele Burastero attached at Appendix A and the receipt of the deposit of the hybridoma attached at Appendix B. The declaration states that the deposit was made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent. Applicants submit that the declaration and deposit receipt attached satisfy the deposit requirements under 37 CFR 1.808. As such, Applicants respectfully request the reconsideration and withdrawal of this rejection with respect to claims 23-28.

Applicants further note that the Examiner has included an Examiner's claim interpretation section on p. 6 of the Office Action. It is unclear to Applicants why the Examiner has included this section or how it relates to the § 112 rejection. However, Applicants maintain that the claim terms are as desribed within the specification on p. 28 and should in no way be limited to Examiner's notation of what the term "antibody" represents.

***Rejection under 35 U.S.C. § 102***

***Kang***

The Examiner has rejected claims 23-24 and 28 under 35 U.S.C. § 102(b) as being anticipated by Kang et al., *J. Virol.*, Vol. 68, No. 9, pp. 5854-5862 (1996) ("Kang"). See Office Action at p. 7. Claim 24 depends from independent claim 23. Claim 28 depends from independent claim 26.

The specification describes antibodies which were raised against HIV envelope complexes expressed on fixed cells comprising an HIV envelope complex complexed with CD4 receptor wherein the envelope is encoded by gp160. See p. 8 of the specification. More specifically the fixed cells express a polypeptide proteolytically cleaved into gp 120 and gp 41 subunits. See p. 13 of the specification. The subunits combine to form an intrinsically unstable polymeric complex which is maintained on the whole cell. See p. 13 of the specification. Subsequent binding of the CD4 receptor to the oligomeric complex enables the exposure of neutralizing epitopes which are not exposed on conjugates which comprise monomeric HIV envelope protein gp 120. See p. 3 of the specification. Therefore, several neutralizing epitopes are only present in the native oligomeric form of the envelope protein (not the monomeric form).

See p. 3 of the specification. Furthermore, several neutralisation epitopes will be exposed on the gp120 monomer but will be hidden in the oligomeric complex. See p. 2 of the specification. The antibodies described in the specification are immune specific to this native oligomeric complex and are therefore different to previously described antibodies which are immune specific to the soluble gp120/CD4 complex (or its separate components gp120 and CD4). See p. 2 of the specification.

Claim 23 relates to an isolated or synthesized antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor. Claim 26 relates to a hybridoma cell line having the identifying characteristics of the cell line deposited with the Advanced Biotechnology Center Inter Lab Cell Line Collection (CBA ICLB) under Deposit number PD03002 wherein the hybridoma produces DB-81.

Kang describes antibodies produced by immunizing animals with soluble CD4-gp120 complex (i.e. conjugates with monomeric HIV envelope protein gp120). See p. 5855 of Kang. Kang does not describe an isolated or synthesized antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor. Kang also does not describe a hybridoma cell line having the identifying characteristics of the cell line deposited with the Advanced Biotechnology Center Inter Lab Cell Line Collection (CBA ICLB) under Deposit number PD03002 wherein the hybridoma produces DB-81.

Since claims 24 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not anticipated by Kang for at least the reasons described above. Applicant respectfully requests reconsideration and withdrawal of this rejection.

***Devico***

The Examiner has rejected claims 23-24 and 28 under 35 U.S.C. § 102(b) as being anticipated by Devico et al., *Virol.*, Vol. 218, pp. 258-263 (1996) ("Devico"). See Office Action at p. 7. Claim 24 depends from independent claim 23. Claim 28 depends from independent claim 26.

Devico describes antibodies produced by immunizing mice with cross-linked soluble CD4-gp120 complex. See p. 584 of Devico. Devico does not describe an isolated or synthesized antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp

160 and further wherein the envelope is complexed with a CD4 receptor. Devico also does not describe a hybridoma cell line having the identifying characteristics of the cell line deposited with the Advanced Biotechnology Center Inter Lab Cell Line Collection (CBA ICLB) under Deposit number PD03002 wherein the hybridoma produces DB-81.

Since claims 24 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not anticipated by Devico for at least the reasons described above. Applicant respectfully requests reconsideration and withdrawal of this rejection.

***Konopka***

The Examiner has rejected claims 23-24 and 28 under 35 U.S.C. § 102(b) as being anticipated by Konopka et al., *J. General Virology,* Vol. 76, pp. 669-679 (1995) ("Konopka"). See Office Action at p. 8. Claim 24 depends from independent claim 23. Claim 28 depends from independent claim 26.

Konopka describes a monoclonal antibody "raised in mice immunized with soluble CD4-gp120 complex." See p. 670 of Konopka. Konopka does not describe an isolated or synthesized antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor. Konopka also does not describe a hybridoma cell line having the identifying characteristics of the cell line deposited with the Advanced Biotechnology Center Inter Lab Cell Line Collection (CBA ICLB) under Deposit number PD03002 wherein the hybridoma produces DB-81.

Since claims 24 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not anticipated by Konopka for at least the reasons described above. Applicant respectfully requests reconsideration and withdrawal of this rejection.

***Sullivan***

The Examiner has rejected claims 23-24 and 28 under 35 U.S.C. § 102(b) as being anticipated by Sullivan et al., *J. Virology,* Vol. 72(6), pp. 4694-4703 (1998) ("Sullivan"). See Office Action at p. 8. Claim 23 depends from independent claim 23. Claim 28 depends from independent claim 26.

Sullivan describes "two cross-competing monoclonal antibodies, 17b and CG10" which were derived from "Epstein-Barr virus (EBV) transformation pf peripheral blood B cells obtained from an asymptomatic HIV-1 infected patient" and "immunization with HIV-1 gp120

glycoprotein from the T-cell line-tropic IIIB strain complexed with sCD4" respectively. See Abstract, p. 4696 and p. 4698 of Sullivan. Sullivan does not describe an isolated or synthesized antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor. Sullivan also does not describe a hybridoma cell line having the identifying characteristics of the cell line deposited with the Advanced Biotechnology Center Inter Lab Cell Line Collection (CBA ICLB) under Deposit number PD03002 wherein the hybridoma produces DB-81.

Since claims 24 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not anticipated by Sullivan for at least the reasons described above. Applicant respectfully requests reconsideration and withdrawal of this rejection.

***Thali***

The Examiner has rejected claims 23-24 and 28 under 35 U.S.C. § 102(b) as being anticipated by Thali et al., *J. Virology,* Vol. 67(7), pp. 3978-88 (1993) ("Thali"). See Office Action at p. 8. Claim 24 depends from independent claim 23. Claim 28 depends from independent claim 26.

Thali describes "17b and 38d monoclonal antibodies, which were derived from different HIV-1 infected individuals ...." See p. 3979 of Thali. Thali does not describe an isolated or synthesized antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor. Thali also does not describe a hybridoma cell line having the identifying characteristics of the cell line deposited with the Advanced Biotechnology Center Inter Lab Cell Line Collection (CBA ICLB) under Deposit number PD03002 wherein the hybridoma produces DB-81.

Since claims 24 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not anticipated by Thali for at least the reasons described above. Applicant respectfully requests reconsideration and withdrawal of this rejection.

***Kwong***

The Examiner has rejected claims 23-24 and 28 under 35 U.S.C. § 102(b) as being anticipated by Kwong et al., *Nature,* Vol. 393, pp. 648-659 (1998) ("Kwong"). See Office Action at p. 8. Claim 24 depends from independent claim 23. Claim 28 depends from independent claim 26.

Kwong describes a "17b antibody [which] is a broadly neutralizing human monoclonal isolated from the blood of an HIV-infected individual." See p. 654 of Kwong. Kwong does not describe an isolated or synthesized antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor. Kwong also does not describe a hybridoma cell line having the identifying characteristics of the cell line deposited with the Advanced Biotechnology Center Inter Lab Cell Line Collection (CBA ICLB) under Deposit number PD03002 wherein the hybridoma produces DB-81.

Since claims 24 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not anticipated by Kwong for at least the reasons described above. Applicant respectfully requests reconsideration and withdrawal of this rejection.

***LeCasse***

The Examiner has rejected claims 23-24 and 28 under 35 U.S.C. § 102(b) as being anticipated by LaCasse et al., *Science,* Vol. 283, pp. 357-362 (1999) ("LaCasse"). See Office Action at p. 9. Claim 24 depends from independent claim 23. Claim 28 depends from independent claim 26.

LaCasse describes using whole cells expressing the HIV envelope "frozen" (by chemical fixation) at random intermediate stages of fusion with cells expressing the receptor complex. See Abstract of LaCasse. LaCasse describes using a "functioning envelope protein [] derived from a T lymphocytotropic P1 virus ..." also known as 168P. See footnote 8 and p. 358 of LaCasse. Applicants wish to note that a retraction has been published for the LaCasse reference (see Nunberg, *Science*, Vol. 296, p. 1025 (2002), attached at Appendix C) which states that the neutralization of primary isolates of HIV described in the LaCasse was due to a specific cytotoxic effect of the complex sera rather than the antibodies themselves.

LaCasse does not describe an isolated or synthesized antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor. LaCasse also does not describe a hybridoma cell line having the identifying characteristics of the cell line deposited with the Advanced Biotechnology Center Inter Lab Cell Line Collection (CBA ICLB) under Deposit number PD03002 wherein the hybridoma produces DB-81.

Since claims 24 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not anticipated by LaCasse for at least the reasons described above. Applicant respectfully requests reconsideration and withdrawal of this rejection.

***Gaudain***

The Examiner has rejected claims 23-25 and 28 under 35 U.S.C. § 102(b) as being anticipated by Gaudain et al., *Nature Medicine,* Vol. 3, pp. 1389-1393 (1997) ("Gaudain"). See Office Action at p. 9. Claims 24 and 25 depend from independent claim 23. Claim 28 depends from independent claim 26.

Gaudain describes a "human monoclonal antibody (mAB) IgG1b12 produced from an immune phage display library ... which recognizes a discontinuous epitope overlapping the CD4bs on HIV-1 gp120 ...." See p. 1392 of Gaudain. Gaudain does not describe an isolated or synthesized antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor. Gaudain also does not describe a hybridoma cell line having the identifying characteristics of the cell line deposited with the Advanced Biotechnology Center Inter Lab Cell Line Collection (CBA ICLB) under Deposit number PD03002 wherein the hybridoma produces DB-81.

Since claims 24, 25 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not anticipated by Gaudain for at least the reasons described above. Applicant respectfully requests reconsideration and withdrawal of this rejection.

***Dimitrov***

The Examiner has rejected claims 23-25 and 28 under 35 U.S.C. § 102(b) as being anticipated by Dimitrov et al., *J. Human Virol.,* Vol. 5, No. 1, Abstract 118 (2002) ("Dimitrov"). See Office Action at p. 9. Claim 23 is an independent claim. Claim 28 depends from independent claim 26.

Dimitrov describes using a phage display library to identify human monoclonal Fabs "which inhibited cell-cell fusion mediated by Envs of primary isolates from different clades ...." Dimitrov also describes "a novel potent broadly neutralizing human monoclonal antibody Fab, X5, which binds with high affinity to gp120 alone and with even higher affinity to its complex with CD4."

Dimitrov does not describe an isolated or synthesized antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor. Dimitrov also does not describe a hybridoma cell line having the identifying characteristics of the cell line deposited with the Advanced Biotechnology Center Inter Lab Cell Line Collection (CBA ICLB) under Deposit number PD03002 wherein the hybridoma produces DB-81.

Accordingly, claim 23 is not anticipated by Gaudain. Since claim 28 depends from claim 26, claim 28 is also not anticipated by Gaudain for at least the reasons described above. Applicant respectfully requests reconsideration and withdrawal of this rejection.

***Rejection under 35 U.S.C. § 102/103***

The Examiner has rejected claims 23-25 and 28 under 35 U.S.C. § 102(e) as being anticipated by, or in the alternative, under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 7,223,844 to Dimitrov et al ("Dimitrov II"). See Office Action at p. 10. Claims 24 and 25 depend from independent claim 23. Claim 28 depends from independent claim 26.

Dimitrov II describes using "purified complexes containing HIV Env together with the cell-surface HIV receptor CD4 and an HIV co-receptor, e.g., CCR5 or CXCR4, can be used to identify and isolate antibodies, and active fragments thereof, which display broadly neutralizing activity against multiple genetic subtypes of HIV." See col. 2, lines 3-10 of Dimitrov II. Dimitrov II does not teach or suggest an isolated or synthesized antibody immunospecific for a fixed cell that includes an HIV envelope complex encoded by gp 160 and further wherein the envelope is complexed with a CD4 receptor. Dimitrov II also does not teach or suggest a hybridoma cell line having the identifying characteristics of the cell line deposited with the Advanced Biotechnology Center Inter Lab Cell Line Collection (CBA ICLB) under Deposit number PD03002 wherein the hybridoma produces DB-81.

Since claims 24, 25 and 28 depend from claims 23 and 26 respectively, claims 24 and 28 are not patentable over Dimitrov II for at least the reasons described above. Applicant respectfully requests reconsideration and withdrawal of this rejection.

## CONCLUSION

Applicant believes that the claims are in condition for allowance.

A petition for a three month extension of time is attached.

Should any fees be required by the present Reply, the Commissioner is hereby authorized to charge Deposit Account 19-4293.

Respectfully submitted,

Date: 4-2-08

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